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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 03/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,853	ANDREWS ET AL.	
	Examiner	Art Unit	
	Thai-An N Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *21,22 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20, 23-25, 27 and 28* is/are rejected.

7)☒ Claim(s) *2-10 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The prior Office action, mailed 1/28/04, is withdrawn. A new time period for response has been restarted with the mailing of this Office action.

1) In a telephonic conversation with Barbara McDowell, on November 4, 2003, it was brought to the Examiner's attention that the claims examined in the prior Office action, mailed 9/12/03, Paper No. 10, did not include claims that were amended under Article 19. The instant Office action includes the amendments to the claims under Article 19.

2) In a telephonic conversation with Michelle Walters on 2/5/04 [see attached interview summary] it was noted that claim 28 was inadvertently left out of the prior Office action. Thus, this Office action includes claim 28.

Claims 1-28 are pending. Claims 1-20, 23-25, 27 and 28 are under current examination. Claims 21, 22 and 26 are withdrawn.

Election/Restrictions

Claims 1-20, 23-25, 27 and 28 are found to correspond to Groups I, III and IV of the Restriction requirement mailed 5/27/03, Paper No. 8. Applicants' election with traverse of Group I in Paper No. 9 is acknowledged. The traversal is on the ground(s) that Groups I, III and IV all share the same special technical feature, which is the defined content of the cell nucleus and cytoplasm. See pp. 1-2, bridging ¶ of Applicants' Response filed 6/27/03, Paper No. 9. Applicants' Arguments are

found to be persuasive. As such, Groups I, III and IV will be examined together. Claims 1-20, 23-25, 27 and 28 are under current examination.

Claims 21, 22 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Claim Objections

Claims 2-10 are objected to because the claims all begin with "A cell according to claim ...". This is inappropriate because there is only one cell that the claim refer to. This objection can be overcome by using the language, "The cell according to claim ...".

Claim 9 is objected to because of the following informalities: the term *pluripotential* is misspelled in line 2 of the claim. Appropriate correction is required.

Claim 10 is objected to because the term *characterized* is misspelled in line 1 of the claim. Appropriate correction is required.

Claim 28 is objected to because the claim begins with, "A method according to claim 17 ..." This is inappropriate because there is only one method that the claims refers to. This objection can be overcome by the recitation of, "The method according to claim 17 ...".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 and 23 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to a cell having a single nucleus, wherein the cell possesses at least one pluripotential characteristic, which characteristic includes the ability to differentiate into at least two selected tissue types, which cell comprises either (i) at least part of the cytoplasm derived from an embryonal teratocarcinoma cell, or (ii) a cytoplast from a teratocarcinoma cell, and which cell has its nucleus obtained from a differentiated somatic cell and only contains the genome derived from the differentiated somatic cell. This is non-statutory because the claimed cells encompass any somatic cell that has been differentiated from an embryonic teratoma, or a naturally occurring teratoma. A cell that has been differentiated from an embryonic teratoma would have at least part of its cytoplasm derived from a embryonic cell, and because it was differentiated, the nucleus of the cell would only contain the genome of a differentiated somatic cell. The recitation of "isolated" would obviate this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20, 23-25, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cells and methods for preparing cells that express Oct4, wherein the cell comprises either (i) at least one part of they cytoplasm derived from an embryonal teratocarcinoma cell, or (ii) a cytoplast from a teratocarcinoma cell, and the cell has its nucleus obtained from a differentiated somatic cell and only contains the genome derived from the differentiated somatic cell, does not reasonably provide enablement for cells and methods of making cells which possess at least one pluripotent characteristic, which includes the ability to differentiate into at least two selected tissue types. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to a cell having a single nucleus, wherein the cell possesses at least one pluripotential characteristic, which characteristic includes the ability to differentiate into at least two selected tissue types, which cell comprises either (i) at least part of the cytoplasm derived from an embryonal teratocarcinoma cell, or (ii) a cytoplast from a teratocarcinoma cell, and which cell has its nucleus obtained from a differentiated somatic cell and only contains the genome derived from the differentiated somatic cell, methods of preparation of a

cytoplasmic part for use in the production of such cells, methods of preparing such cells, cell cultures, therapeutic compositions and tissue types or organs comprising such cells.

The specification teaches the generation of pluripotent cells comprising at least part of the cytoplasm from a teratocarcinoma cell, and the nucleus of a somatic cell. The specification teaches that teratomas [tumors which contain a wide range of more or less organized tissues] typically occur as gonadal tumors [see p. 5, lines 16-24]. These embryonic carcinoma [EC] cells were found to resemble early embryonic cells and it was found that EC cells were able to generate a range of differentiated cells. See pp. 6-7. The specification teaches the generation of a cybrid [a cell comprising at least a part of its cytoplasm from an EC cell] combined with the nucleus of a somatic cell, wherein the cybrid has pluripotent characteristics that allow it to differentiate into at least one selected tissue type. See p. 10.

The specification specifically teaches the preparation of mouse thymocytes, which were then fused using polyethylene glycol [PEG] to human EC cells. The fused cells were plated and after 2 days, the non-attached cells were aspirated. The remaining cells were harvested and RNA isolated and quantified. The cells were then analyzed for the expression of Oct-4 by PCR. See p. 18-20. The specification teaches the enucleation of EC cells by cytochalasin B to generate cytoplasts. The specification teaches that re-programmed embryonic stem [RPES] cells can be

made by fusing two or more cells of different origins. Following the production of the RPES cells, additional methods are required to propagate the cells, characterize their properties, and induce them to differentiate into required somatic cell types. See p. 22-23, 25-31. The specification teaches that a large range of somatic cells may be used as nuclear donors, and that a large number of human EC cell lines have been isolated which can be used in the claimed methods. See pp. 24-25. The specification teaches that human Oct4 expression was detected in the thymocyte fused cells, as well as in the mock fusion experiment, which is consistent with the human Oct4 expression in the human EC cells. It was found that mouse Oct4 was detected in only the human-mouse fused cells. See pp. 33-34. The specification further teaches that in a second experiment, where human 2102Ep and TERA1 EC cells were fused with mouse thymocytes, mouse Oct4 was detected in the fusion of the 2102Ep cells, suggesting that the TERA1 cytoplasm did not achieve reprogramming. See p. 34, lines 1-4.

The specification fails to provide teachings or guidance with regard to the claimed invention to show that the cells produced by the claimed method are pluripotent, as required by the claims. Note that the product claims (claims 1-12, 23 and 27) have been included in this rejection because they encompass pluripotent cells made by the claimed method. The specification clearly teaches that the claimed methods would be used to produce pluripotent cells. See p. 7, lines 17-18, for example. However, the only teachings provided by the specification show that

the expression of mouse Oct4 in the experiments involving the fusion of the human EC cell line, 2102Ep and mouse thymocytes which the specification concludes indicates that the mouse thymocytes were reprogrammed. The specification teaches another human EC cell line, TERA1, was unable to reprogram the mouse thymocytes, as shown by the lack of expression of mouse Oct4. As such, the specification teaches only one example to show reprogramming in mouse thymocytes, as evidenced by the expression of Oct4. However, it is known in the art that the expression of Oct4 is not necessarily an indicator of pluripotency. For example, Monk and Holding [**Oncogene**, 20:8085-8091 (2001)] found that Oct4 is expressed in human tumors. See *Abstract.* Monk & Holding compare the expression of embryo-specific genes in tumor and normal tissues [see Figure 3] and found that the known embryonic gene, Oct4, was expressed in the panel of tumors, and at high levels in blastocyst and cancer cells, but at much lower levels in normal tissue. See Figure 5. As such, the art supports that although Oct4 is recognized as an embryonic gene, the mere detection of expression of Oct4 is not an indicator of pluripotency, because tumor tissues, as well as normal tissues, express Oct4.

The specification further teaches that primate ES cells exhibit a range of characteristics or markers that are associated with pluripotency. For example, specific cell surface markers [SSEA-3 (+), SSEA-4 (+), TRA-1-60 (+), TRA-1-81 (+)], have stable karyotypes, continue to proliferate in culture in an undifferentiated state, and have the ability to differentiate into all three embryonic germ layers [see

p. 3, lines 16-23]. Furthermore, the specification teaches that primate ES cell lines show high levels of telomerase activity [see p. 3, lines 25-29], and that a pluripotential characteristic is a chromosomal methylation pattern characteristic of pluripotential cells [pp. 9-10, bridging ¶], and that the cells when introduced into an animal, have the ability to induce tumors into the animal [p. 10, lines 11-13].

However, the specification fails to provide specific teachings or guidance to show that the methods of the claimed invention would, indeed, produce cells that are pluripotent. The specification's showing of mere Oct4 expression in the fused heterokaryons is not enabling, as shown *supra*, that the mere expression of Oct4 is not necessarily indicative of pluripotency. The specification fails to teach that the cells of the claimed invention express specific cell surface markers that are indicative of pluripotent cells, that the cells of the invention show high levels of telomerase activity, are methylated in a pattern characteristic of pluripotent cells, or are able to induce tumors when introduced in an animal, as required by the claims. As such, the specification fails to provide an enabling disclosure for the generation and use of the claimed cells.

It is noted that certain of the claims are directed to methods which generate a nuclear transfer unit, wherein the NT unit is further cultured under conditions to proliferate and expand the NT unit. See part (iii) of claim 15, for example. However, it is well known in the nuclear transfer art that activation of the resulting nuclear transfer unit must take place in order to effect further development;

however, the claims do not provide such steps. Dinnyés *et al.* [**Cloning & Stem Cells**, 4:81-90, 2002] report on the state of the art of somatic cell nuclear transfer state that, "NT is a complex procedure and each step effects the overall efficiency. The unpredictability of the technology due to biological variation of the recipient oocytes and the donor cells is difficult to control. Therefore, standardization of the steps is important in order to obtain consistent results." [See p. 83, 1st column, 2nd full paragraph]. With particular regard to the importance of the activation of oocytes, Dinnyés *et al.* state that, "In NT, the lack of sperm-induced fertilization steps necessitate the application of an artificial activation in order to trigger further development." [See p. 83, 2nd column, last paragraph].

The specification fails to provide teachings to show the exemplified methods would produce a cell with a pluripotential characteristic, which includes the ability to differentiate into at least two selected tissue types, as required by the claims. The specification further fails to show that using an EC cell as a cytoplast recipient in a nuclear transfer method would result in the generation of cells which would be considered pluripotent. For example, the specification fails to teach or provide guidance to show that the RPES cells of the instant invention would further develop such that they could differentiate. The state of the art of nuclear transfer teaches that in successful NT methods, the recipient cell [cytoplast] can be an oocyte, fertilized zygote or two-cell embryo, cells which are able to support further

development of the NT unit. For example, Campbell *et al.* [**Cloning & Stem Cells**, 3(4):201-208, 2001] teach that:

> *Oocytes, fertilized zygotes, and two-cell embryos have been used as cytoplast recipients for NT. In general, oocytes arrested at metaphase of the second meiotic division have become the cytoplast of choice. At this point in oocyte development, the genetic material is arranged upon the meiotic spindle and is easily removed using mechanical means ... The use of fertilized zygotes as cytoplast recipients has been reported in mouse, cattle and pigs. In all three species, development of embryos constructed using zygotes as cytoplast recipients was low, and on the whole, restricted to the exchange of pronuclei, suggesting that factors essential for successful development are removed with the pronuclei.* See p. 202, 2nd column, ***The Recipient Cell or Cytoplast.***

The instant invention requires that the cells produced by the claimed method be able to differentiate into at least two tissue types, thus, the cell requires further development, which, as supported by the art, would be possible utilizing, for example, an oocyte. Although the specification provides general teachings with regard to how the fused EC/differentiated cell would be grown and selected, see pp. 28-29, the specification fails to show that an EC would support further development, such that the cells would pluripotent and be able to differentiate into at least two selected tissue types.

Furthermore, with regard to claim 5, the claim is directed to a cell comprising at least part of the cytoplasm derived from an EC combined with a nucleus of a differentiated cell, wherein the cell express Oct 4. The claim, as written, describes a nuclear transfer unit wherein the NT unit expresses Oct4. The specification fails

to provide teachings or guidance to show that the nuclear transfer unit, as claimed, would indeed express Oct-4. For example, the specification teaches the heterokayon fusion of human EC cells and mouse thymocytes, the cells were first fused and then plated and incubated for 2 days. After 2 days, the non-attached cells were aspirated and the remaining cells were analyzed by PCR for the expression of Oct-4. See pp. 15-16. The specification teaches that the expression of Oct-4 indicates the reprogramming of a somatic cell nucleus to an ES/EC cell like state [see p. 28, lines 16-19]. The specification teaches that, "Following fusion to combine a differentiated cell and an ES/EG cell, with prior or subsequent removal of the ES/EG cell nucleus, it is necessary to provide appropriate conditions for the re-programming of the differentiated cell nucleus and the subsequent proliferation of the resulting RPES [Reprogrammed Embryonic Stem] cells." See p. 24, lines 15-18. As such, the specification provides support for cells cultured from the NT unit that express Oct-4, however, the specification fails to provide sufficient teachings or guidance to show that the nuclear transfer unit itself would express Oct-4, as the specification clearly teaches the growth and proliferation of the original nuclear transfer units for 2 days before analysis for Oct-4 expression.

Accordingly, in view of the lack of specific teaching or guidance provided by the specification with regard to the pluripotency of the cells produced by the nuclear transfer methods, other than the mere expression of Oct4, the state of the art, which teaches that Oct4 is expressed in normal, cancerous and embryonic tissues,

the requirement for activation of the nuclear transfer unit to produce a successful nuclear transfer, it would have required undue experimentation for one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1, as written, is indefinite. The claim recites that the cell has, "the ability" to differentiate into at least two selected tissue types. See lines 2-3 of the claim. This describes a latent property, and it is unclear whether this actually occurs or not. "The ability" implies a latent property and the conditions for the latent property must be clearly defined. Therefore, it is unclear if the latent property is ever obtained. The claim is further unclear because it states that the cytoplasm of the cell is "derived from" an embryonal teratocarcinoma. It is unclear how the cytoplasm is derived, for example, has it been modified? The claim recites that the cell contains a nucleus that has been obtained from a differentiated somatic cell and only contains the genome derived from the differentiated somatic cell. This is unclear because if the nucleus only contains the genome of a somatic cell, are there no transcription factors and other factors that are normally found in the nucleus of a cell? Further, how is the genome "derived" from a somatic cell? Has it

been reprogrammed, or is it a differentiated cell nucleus, or has the genome in some way been modified, for example, by mutation? Clarification and/or amendment to the claim is requested. Claims 2-15, 20, 23-25, and 27 depend from claim 1.

Claim 3 is indefinite. The claim recites that the cell has "the capacity" to proliferate in line 2 of the claim. "The capacity" describes a latent property and it is unclear if this property occurs or not.

Claim 5, as written, is indefinite. The claim recites that the cell has "the capacity" to proliferate [see lines 1-2 of the claim]. "Capable of" describes a latent property, and it is unclear whether this property occurs or not.

Claim 9, as written, is vague. The claim recites that the cell, "includes the presence of a chromosomal methylation pattern characteristic of pluripotential cells". This is unclear because it would not be expected that all types of pluripotent cells would express the same methylation pattern. For example, would adult pluripotent stem cells have the same methylation pattern as other pluripotent stem cells? Clarification and/or amendment to the claim is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-12, 20, 23-25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson [WO 96/22362, published 25 July 1996].

The claims are directed to a cell having a single nucleus, wherein the cell possesses at least one pluripotential characteristic, which characteristic includes the ability to differentiate into at least two selected tissue types, which cell comprises either (i) at least part of the cytoplasm derived from an embryonal teratocarcinoma cell, or (ii) a cytoplast from a teratocarcinoma cell, and which cell has its nucleus obtained from a differentiated somatic cell and only contains the genome derived from the differentiated somatic cell, wherein the cell

Thomson teach the isolation and purification of primate embryonic stem cells that are capable of indefinite proliferation *in vitro* in an undifferentiated state, are capable of differentiation to derivatives of all three embryonic germ layers, and maintain a normal karyotype throughout prolonged culture. Thomson teach that tumors formed after injection of rhesus ES cells into the hindleg muscles of SCID mice [see Figure 5]. These tumors were analyzed and it was found that the tumors ontained cartilage, smooth muscle and striated muscle, stratified squamous epithelium with hair follicles, neural tube with ventricular, intermediate and mantle layers, ciliated columnar epithelium, villi and mucus-secreting goblet cells. See pp. 21-22, bridging ¶.

Thomson teaches the claimed invention because the claims require that the cells have the ability to differentiate into at least two tissue types. Further, the

teratomas as taught by Thomson have at least part of the cytoplasm derived from an embryonal teratocarcinoma cell, and a nucleus that contains a genome derived from a differentiated somatic cell. The cytoplasm of the Thomson's teratomas would be "derived" from an embryonal teratocarcinoma cell, and a nucleus that is "derived" from a differentiated somatic cell could be a reprogrammed cell nucleus, for example. The claimed properties of the cells [for example, that the cells have the ability to proliferate in a culture in an undifferentiated state] is an inherent property of the cells. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Note that claim 27 is directed to a kit comprising the cells of claim 1, instructions with respect to maintenance of the cell in culture, and optionally factors required to induce differentiation of the cell into at least one desired tissue type or organ.

In re Gulack (CAFC) 217 USPQ 401 relates to a measuring cup. In the case of *In re* Gulack, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the

kit remain fully functional absent the printed instructions for use. Thus, the instructions for use included in a kit or article of manufacture constitute "intended use" for that kit or article of manufacture. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

> Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

In the instant case, the claim is drawn to a kit comprising the cells of claim 1, instructions with respect to maintenance of the cell in culture, and optionally factors required to induce differentiation of the cell into at least one desired tissue type or organ. The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). Therefore, the kit is unpatentable over the prior art because they function equally effectively with or without the instructions, and accordingly no functional relationship exists between the instructions for use and the kit components.

Accordingly, Thomson anticipates the claimed invention.

Claims 1, 4, 6, 11, 20, 23, 24, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Warejcka *et al.* [J. of Surg. Res., 62:233-242 (1996)].

Warejcka teach that stem cells were isolated from rat hearts. These cells were then cultured and then allowed to differentiate by application od dexamethasone. See p. 234, 1st column. The differentiated cells were then analyzed for the identification of phenotypes histochemically and immunochemically. Warejcka teach that differentiation of the cells resulted in cartilage nodules, endothelial cells, adipocytes, smooth muscle cells and putative cardiomyocytes. See *Abstract* and pp. 235-236.

Warejcka teach the claimed invention because the cells only require the ability to differentiate into two selected cell types. Furthermore, the cells, as claimed merely require that the cytoplasm of the cells be "derived from" an embryonal teratocarcinoma cell, and that the nucleus be "derived" from a differentiated somatic cell. Thus, a cell, as described by Warejcka anticipates the claimed cells because one of skill in the art would not be able to tell the difference between cells that had cytoplasm derived from an embryonal teratocarcinoma cell, and the cells of the art. Note that claims 24, 25 and 27 recite the intended use of the cells, which does not impart patentable weight. See *supra*.

Accordingly, Warejcka anticipates the claimed invention.

Claims 1-12, 20, 23-25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Pera *et al.* [**Differentiation**, 89:10-23 (1989)].

Pera teach the isolation and characterization of the human teratoma cell line, GCT 27. See *Abstract.* Pera teach that cytogenetic analysis, growth properties and marker expression of the cells were analyzed. See pp. 10-11. It was found that intramuscular or subcutaneous injection of the cells resulted in the formation of embryonal teratocarcinomas. Various cell tissues were found upon analysis, including epithelial tissues, primitive mesenchymal cells, and neuroectodermal epithelium. See Figure 3 and pp. 13-14. The marker expression of the cells was analyzed. See Table 2.

Pera anticipate the claimed invention because the human teratoma cell line taught by Pera have at least part of the cytoplasm derived from an embryonal teratainoma cell, and because the nucleus of the cell need only be "derived" from a differentiated somatic cell, such a cell could be a reprogrammed cell, which would be identical to that of the cells taught by Pera. Note that further properties of the cells, such as the ability of the cells to proliferate in culture in an undifferentiated state, would be an inherent property of the cells. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claims 24, 25 and 27 recite the intended use of the cells, and it is reiterated that the intended use does not impart patentable weight. See *supra*.

Accordingly, Pera anticipate the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (571) 272-0548. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

TNT
Thaian N. Ton
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